THE AMERICAN
JOURNAL OF PHARMACY

FEBRUARY, 1914

THE OIL OF ARGEMONE MEXICANA.

By Kshitibhushan Bhaduri, M.Sc.

Historical.

This is an American plant, which has run wild all over India. It may easily be known by its glaucous, prickly, thistle-like leaves, bright yellow flowers, and milky juice. The latter is used as an application to ulcers and in combination with the juice of Aristolochia bracteata is given internally in syphilis and gonorrhœa. In the Concan the juice with milk is given in leprosy. The seeds and oil have been used by European physicians. The oil in doses from 30 to 60 drops is a valuable remedy in dysentery and other affections of the internal canal. Fluckiger found 4 to 5 gms. to have a mild purgative effect. An extract made from the whole plant has been found to have an aperient action and the milky juice to promote the healing of indolent ulcers.

The oil used for examination was obtained by pressing the crushed seeds in a screw press in the laboratory in presence of the author. The chances of adulteration were thus avoided.

Experimental.

Some of the crushed seeds were submitted to steam distillation; the distillate had a slight opalescence and a very pungent odor, but no oil came over.

47.1176 gms. of the crushed seeds were exhausted in a Soxhlet apparatus with petroleum ether, the latter evaporated off when 10.4966 gms. of a thin brown colored oil was left behind. Hence the percentage of oil is 22.3. According to Charbonnier the seeds contain 36 per cent. of oil.

The petroleum ether extract has a pale greenish-yellow color with a green fluorescence, if it be evaporated at the ordinary temperature, the oil left behind has an olive green color. If this be

either left exposed to the atmosphere or heated on the water bath it gradually acquires a rich brown color. If it be still further heated the color deepens and it diffuses a very intense odor, like that of the juice of the fresh plant.

The pressed oil was of a deep brown color, had a mild odor and was tasteless. The freshly obtained oil was very thin, but on keeping it gradually thickened. Crossley and Le Sueur (*Journ. Soc. Chem. Ind.*, 1898, 991) say the fresh oil is of orange color and has a slight but distinctive smell.

The mixed fatty acids had a paler color and were very thin.

The oil on keeping exposed to the atmosphere or on treatment with an oxidizing agent deposited a very small quantity of a red crystalline substance (M.P. 172° C.).

The oil gradually thickened with the lowering of temperature, until at 17° C. the clear liquid became turbid, the temperature remained constant for a little time at 16° C. Charbonnier's oil remained clear at —8° C. and Fluckiger's oil at —6° C.

The specific gravity was determined at two different temperatures, at 28° C. and at the boiling point of water. In the former case it was 0.9117 and at the latter it was 0.9007. Charbonnier obtained a specific gravity of 0.920, Fluckiger 0.919 at 16.5° C. and Crossley and Le Sueur 0.9247–0.9259 at 15.5° C.

The refractive index obtained with a Pulfrich's refractometer was 43° 34′ at 32° C. or 1.46552. With a butyro refractometer Crossley and Le Sueur obtained at 40° C. a refractive index of 62.5.

The oil and absolute alcohol were miscible in any extent. For the determination of its solubility in dilute alcohol the following method was adopted. In a stoppered graduated tall cylinder a measured volume of oil was introduced, to this a known volume of alcohol was added and then water added drop by drop with continuous shaking till a permanent turbidity was obtained. The total volume was read off and from this when the volume of oil and alcohol was subtracted the volume of water added was obtained.

TABLE OF SOLUBILITY IN ALCOHOL OF DIFFERENT STRENGTH AT 32°C.

Oil.	Water.	Alcohol.
10	9	12
10	15	20
10	22	32
10	28	42
11	24	42
15	24	45

116.4 c.c. of $\frac{N}{10}$ alcoholic potash (calculated) were required for the saponification of 3.4828 gms. of oil; hence the saponification value is 185.5. The saponification obtained by Crossley and Le Sueur is 187.8–190.3.

The oil was acetylated by boiling with acetic anhydride and purified, then dried with anhydrous Sodium Sulphate. 3.23 gms. of oil thus obtained required 122 c.c. (calculated) of $\frac{N}{10}$ potash for complete saponification. The saponification value of the acetylated oil was 213.4 and deducting from this 185.5, the saponification value, we got 27.9 as the acetyl value.

The oil contained a large proportion of free fatty acid for which determination 3.5998 gms. of oil was dissolved in 50 c.c. of neutralized alcohol and a little phenolphthalein solution added and titrated with $\frac{N}{10}$ alkali. It was found that 94.3 c.c. was necessary for neutralization, hence the acid value is 146. Two specimens of oil were examined by Crossley and Le Sueur who found 6.0 and 83.9 as the acid value.

In the aqueous solution left after the decomposition of the soap with an acid, the presence of the following fatty acids was proved (1) acetic acid proved by the Cacodyl test and (2) valeric acid by the formation of the ester.

In a weighed flask 2.3696 gms. of oil was taken and dissolved in 50 c.c. of chloroform, and Bromine gradually added till no further absorption took place. It was then evaporated off on the water bath and dried. The weight of the brominated oil now was 4.7912 or the increase in weight was 102.2 per cent. This is the bromine value.

The iodine value of the oil is 106.7. That obtained by Crossley and Le Sueur is 119.91–122.5.

2.7 gms. of oil was saponified, then decomposed with dilute sulphuric acid and submitted to steam distillation. 0.33 c.c. of $\frac{N}{10}$ alkali was required for neutralization of 100 c.c. distillate. Therefore the Reichert-Meisel value is 0.61.

From 1.8426 gms. of oil the author obtained 1.7295 gms. of a mixture of insoluble fatty acids and unsaponifiable matters. The Hehner's value is 94.02. The above authors obtained 95.07.

The glycerol was estimated by the Benedikt and Zsismondy process. This consists in oxidizing the glycerol to oxalic acid by

potassium permanganate. From the amount of oxalic acid obtained the weight of glycerol was calculated. It was found to be 15.48 per cent.

6.1996 gms. of oil was saponified, alcohol evaporated off; it was then dissolved in water and extracted with ether. The ethereal extract on evaporation left behind .1418 gm. of residue or the oil contains 2.29 per cent. of unsaponifiable matter.

The elaidin produced by the oil was an orange-colored, dough-like mass. The reaction was very violent.

When sulphur chloride was added to a solution of equal volume of oil and carbon disulphide a violent reaction ensued, the whole mass frothing up; a very sticky mass was left behind.

When 10 gms. of sulphuric acid was added to 50 gms. of oil the rise of temperature was 65° C. The Maumene test was 65° C.

The rise in temperature on brominating 1 c.c. of oil was 16.5° C.

The oil gave no characteristic color reaction with sulphuric acid even when it was diluted with carbon disulphide. The color was blackish-brown in the former case and in the latter case light brown.

On shaking the oil with nitric acid it acquired a deep brown color and the acid a deep red color. On heating it a violent reaction ensued, a pale orange-colored scum was formed when the whole was allowed to stand over night.

For the determination of oxygen absorption power a quantity of lead was prepared by Livache's method; about a gram of it was spread upon a watch glass and a weighed volume of the oil was spread on it by allowing it to drop on different places. This was weighed. The weights on each successive day were noted till there was no further increase in weight.

Gain in Weight of 1.3437 gms. of Oil.

Days.	Increase in weight.	Per cent. increase.
1st day.	0.269	2.002
2nd day.	0.107	0.8
3rd day.	0.0084	0.6
5th day.	0.0152	1.1
6th day.	0.0059	0.44
8th day.	0.0065	0.48
9th day.	0.0015	0.1
10th day.	No increase.	

Total gain in weight till constant = 5.522.

39 c.c. of the oil was fractionally distilled at 15 mm. pressure when the following fractions were obtained.

Temperature.	Weight of fraction.	Remarks.
215°–217° C.	3.81	Instantly solidified.
217°–224° C.	9.08	Solidified but contained some liquid.
224°–228° C.	9.24	Liquid, on prolonged keeping a few crystals separated out.
228°–231° C.	6.45	Pale brown liquid.
231°–235° C.	2.79	Greenish liquid.

Examination of the Mixed Fatty Acids.

The specific gravity at 28° C. is 0.9065 and at the boiling point of water 0.8889.

2.0688 gms. required for saponification 90.4 c.c. of $\frac{N}{10}$ alkali. The saponification value is 194.

0.40745 gms. of oil absorbed 0.6003 gms. of iodine from a solution of iodine and mercury bichloride in absolute alcohol. The iodine value hence is 147.4.

To find out the neutralization value, 3.6638 gms. of the mixture were diluted with 50 c.c. of neutralized alcohol, a drop of phenolphthalein solution added and titrated with a normal solution of caustic potash. It was found 12.64 c.c. were necessary for this purpose. Hence it follows that 193.2 mgms. of KOH were necessary for the neutralization of one gram of the mixture. The mean molecular weight is found by dividing 56.1 by that found necessary for the neutralization of one gm. of oil.

Let M be the molecular weight and n the weight of KOH in gms.

$$\therefore M = \frac{56.1}{n}$$

now $n = a \times 0.0561$ (a number of c.c.'s of normal KOH).

$$\therefore M = \frac{56.1}{a \times 0.0561} = \frac{1000}{a} = \frac{1000}{3.45} = 289.8.$$

3.3303 gms. of oil gave 2.5847 gms. of liquid fatty acid by the lead-salt-ether process. Therefore, 77 per cent. of the total fatty acid was liquid fatty acid.

It was found that the oil did not contain any stearic acid.

The lactone value of the mixed fatty acid was the difference between the saponification and neutralization values, .8.

The titer test of temperature of turbidity of the mixed fatty acid is 22° C.

The mixed fatty acid contains 8.14 per cent. of lauric acid as was found by fractional distillation of the oil *in vacuo*.

Chemical Laboratory, PRESEDENCY COLLEGE, Calcutta.

AN ASSAY PROCESS FOR QUININE IN TABLETS.

BY SIDNEY F. FIESELMANN, Peoria, Ill.

A rapid method for the quantitative estimation of quinine in tablets, containing no other chloroform soluble constituents, that are not expelled at a temperature of 125° C., which has been successfully used by the author with accurate results, is the following:

Count out a sufficient number of tablets, so as to make the total number represent 10 grains of quinine or quinine salts, based on the quantity claimed on the label. If the quantity stated per tablet cannot be made to come out in a whole number of tablets, take the number of tablets, which contain about 10 grains and make the required correction. Weigh the tablets counted out accurately on an analytical balance. Multiply this weight by two and call it *X* grams. Then powder a sufficient amount of tablets and force all through a number sixty sieve. In case of coated tablets be careful not to loose any particle of the hard coating or parts of tablets during the process of powdering and sifting. Then mix thoroughly after this operation, so as to insure a uniform representative mixture. Weigh up *X* grams of this powder in a 100 c.c. Erlenmeyer flask, add 50 c.c. of chloroform, accurately measured, stopper and shake well. Now add 5 c.c. of ammonia water U. S. P., stopper well and shake thoroughly for 20 minutes. Let stand for about 12 hours in a cool place, with occasional shaking, and decant the chloroform into a separatory funnel, stopper well and allow to stand until separation takes place. Take a 5 cm. plain folded filter paper, on a small 60° glass funnel, moisten with a little chloroform, taking care not to have any chloroform drop into the measuring cylinder or any remaining in the tube of the funnel. Then withdraw enough of the chloroformic solution in the separating funnel and filter the same through the moistened filter paper into a 50 c.c. measuring cylinder until 25 c.c. are obtained.

If this 25 c.c. of filtrate is colorless or of a light straw color, transfer it to a tared beaker of 60–100 c.c. capacity, rinsing the cylinder with three portions of 10 c.c. of chloroform and adding the same to the chloroform solution in the tared beaker. Then evaporate the chloroform carefully on a water bath. If the filtrate is highly colored, from the coating, coloring matter, or resinous substances in the tablets, transfer the same into a clean separatory funnel, rinse out the cylinder as before, adding the same to the chloroform solution in the separatory funnel, and shake out with three portions of normal sulphuric acid, 15, 5, 5 c.c. respectively, each portion diluted with 5 c.c. of distilled water. Collect the combined acid aqueous solution in a clean separatory funnel, add a small piece of red litmus paper, make distinctly alkaline with ammonia water U. S. P. and shake out with three successive portions of 25, 15, and 15 c.c. of chloroform, collecting the same in a tared beaker. After the chloroform has evaporated, redissolve the residue in 5 or 10 c.c. of ether and let evaporate spontaneously.

Finally, place the tared beaker, containing the quinine residue in a drying oven and heat to a constant weight at 125° C., cooling the tared beaker each time in a desiccator before weighing. It usually requires from one to three hours of heating until the weight is constant. The tared beaker should be chemically clean and heated for at least one half hour at 125° C. and cooled in a calcium chloride desiccator, before it is weighed and the chloroformic solution added.

If exactly 10 grains of quinine or the salts of quinine were taken as per label the residue should weigh the following:

For Quinine Alkaloid U. S. P. (Quinine + $3H_2O$)	0.5553 Grams.
For Quinine Bisulphate U. S. P.	0.3830 Grams.
For Quinine Hydrobromide U. S. P.	0.4963 Grams.
For Quinine Hydrochloride U. S. P.	0.5296 Grams.
For Quinine Salicylate U. S. P.	0.4457 Grams.
For Quinine Sulphate U. S. P.	0.4814 Grams.

Tablets containing substances like calcined magnesia as a drying agent, do not filter rapidly by the above method. The water in the ammonia water forms a gelatinous mass with the magnesia, which prevents rapid filtration and sometimes stops it altogether. In that case the following method is suggested. Measure out in a 50 c.c. measuring cylinder, 5 c.c. of spirit of ammonia U. S. P., add a sufficient quantity of chloroform to make exactly 50 c.c. Use

this as a menstruum and follow the other directions as given above omitting the ammonia water. This last method cannot always be used on account of the alcohol in the spirit of ammonia U. S. P., which dissolves more substances than the chloroform would alone and so the residue would not be pure quinine. On the other hand chloroform alone will not dissolve anything but the quinine of the substances usually found in quinine tablets.

In order to obtain sufficient chloroformic filtrate from tablets containing an unusual large quantity of other material and only a small amount of quinine, it may be necessary to increase the chloroformic menstruum from 50 c.c. to 100 c.c. or more, filtering off one half the quantity used, following the instructions given above.

SUTLIFF AND CASE CO., Peoria, Ill.

U. S. P. 1900 MENSTRUA.

By H. C. HAMILTON.

It seems almost superfluous to call attention, at this late date, to certain points in the 8th Revision of the U. S. P. which need correction in the forthcoming 9th Revision. Particularly does it seem unnecessary in view of the fact that the objectionable features to which this article alludes have been pointed out before and by several critics. The excuse for doing so, however, if any is necessary, is that the data here published may be of value to those who have under consideration for the 9th Revision of the Pharmacopœia the menstrua for the extraction of the digitalis series of heart tonics. The menstrua to which we refer are for the preparation of: I. F. E. Digitalis; II. F. E. Squill; III. F. E. Convallaria.

I. The first two of these were referred to by Houghton and Hamilton [1] in the following words:

"3. Fluidextract digitalis, U. S. P. 8th Rev., 48 per cent. alcohol.

"Average potency of eleven samples at time of manufacture 55 H. T. U. per c.c. Three and a half years later 35 H. T. U. Average loss about 10 per cent. yearly.

"A very important point should be noted in this connection; namely, the menstruum adopted in the last U. S. P. for the preparation of fluidextract digitalis is much less desirable than the U. S. P. 7th Revision in at least two respects. Repeated trials show that it is

almost impossible to get a finished product containing the full number of H. T. U. of the standard we had previously adopted, the average being as above stated, 55 H. T. U. per c.c., while with drug of the same quality when the 7th Revision menstruum is employed no difficulty is experienced. Owing to this it was decided to no longer attempt to assay physiologically the 8th Revision product and to take such statement referring to it off the label, but, in order to supply the medical profession with a full strength fluidextract of the drug, it was decided to prepare such with a menstruum containing a larger per cent. of alcohol which could be assayed and so labelled. In the second place the loss in potency of the 8th Revision is about 10 per cent. per year, while with the 7th Revision it is less than one-half as great, or about 4 per cent. The results coincide quite closely with those following the change made in the menstruum for the fluidextract of squill except that the loss in activity was greater in the latter drug, as pointed out by Houghton [2] three years ago. In this paper several methods of physiological assay showed very clearly that a serious mistake had been made in changing to acetic acid as a menstruum. The writers feel certain that any one who has tried the 8th Revision menstruum for fluidextract digitalis has found that it is much less satisfactory from a pharmaceutical point of view, to say nothing of the loss in potency."

To this we wish to add data since obtained on F. E. Digitalis as follows:

Menstruum.	Per cent. Activity.
50 per cent. alcohol	100
80 per cent. alcohol	120

The above samples were prepared from one lot of drug, using 100 grams and extracting until exhausted.

Another small sample of drug carefully extracted by both methods and tested gave results as follows:

with 50 per cent. alcohol	110 per cent. of standard.
with 80 per cent. alcohol	140 per cent. of standard.

A sample of drug extracted with several strengths of alcohol gave the following results:

Menstruum.	Per cent. Activity.
94 per cent. alcohol	90
75 per cent. alcohol	140
62.7 per cent. alcohol	125
50 per cent. alcohol	110

The following table shows the tests of commercial lots of F. E. Digitalis, U. S. P. 8th Rev. (*a*) before and (*b*) after an attempt to improve the quality by concentrating the extract.

Number.	Tested.	Per cent. Activity.
1 (*a*)	8/4/9	85
1 (*b*)	8/19/9	90
2 (*a*)	7/20/9	85
2 (*b*)	8/4/9	85
3 (*a*)	3/4/9	60
3 (*b*)	4/2/9	100
4 (*a*)	1/31/8	80
4 (*b*)	2/8/8	80
5 (*a*)	5/23/7	75
5 (*b*)	6/1/7	83

Further data on 20 samples of the preparation show results of first tests ranging from 50 to 100 per cent. standard and averaging exactly 78 per cent.

The standard referred to is the average activity obtained from 12 lots of crude drug, botanically of first class quality, selected at random and extracted with 62.7 per cent. alcohol, the official menstruum of the U. S. P. 7th Revision. The activity was determined by the frog method described by Houghton [3] as a means of standardizing the heart tonics of the digitalis series. In that article attention was called to the enormous variation in samples of the crude drug for sale on the open market.

The value of such a method is also shown when endeavoring to extract from active material all the therapeutically active substances and to establish by experiments on other than the human subject the relative activity of extracts obtained by means of various menstrua.

The above results speak for themselves, but if additional authority is needed it should be sufficient to note that the menstrua for making tinctures and fluidextracts of digitalis in the official Pharmacopœiæ of the world, specify, almost without exception, a percentage of alcohol in excess of that official in the U. S. P. 8th Revision. The menstruum adopted in 1906 by the Brussels Conference is 70 per cent. alcohol and it is to be hoped that the Revision Committee will be influenced by this in adopting an official menstruum for the 9th Rev. of the U. S. P.

II. As noted before in the abstract from the AMERICAN JOURNAL

OF PHARMACY[1] a mistake was certainly made in adopting for the preparation of F. E. Squill, U. S. P., 8th Rev., a menstruum composed of a 10 per cent. solution of Acetic Acid. This is so far from being ideal for extracting the active substances from Squill bulb that it is practically impossible to prepare an extract representing the activity of the crude drug.

Comparison of the activity of F. E. Squill, U. S. P., 1890 and 1900, was made by Houghton[4] as follows:

"Comparative Strength of Fluid Extract of Squill Prepared from the Same Lot of Drug According to the United States Pharmacopœia of 1890 and 1900:

"1 U.S.P., 1890, 140 per cent. as active as standard fluid extract.
"2 U.S.P., 1890, 140 per cent. as active as standard fluid extract.
"3 U.S.P., 1900, 60 per cent. as active as standard fluid extract.
"4 U.S.P., 1900, 60 per cent. as active as standard fluid extract.

"It may be observed that activity of both products is high as compared with the results given in Table 2. This probably is due to the great care exercised completely to exhaust the drug and to the high quality of the drug.

"In order to meet any objections that might be offered against the results as shown by the special method of assay employed, the work was checked by experiments on dogs showing the comparative activity of the two products in producing changes in the blood-pressure, which is perhaps the most characteristic physiologic action of the members of the digitalis series."

The results of the latter experiments are here recorded in tabular form for more convenient reference.

EXPERIMENT I.

	F. E. Squill, U. S. P., 1890.		F. E. Squill, U. S. P., 1900.	
	Before injection.	After injection.	Before.	After.
Pulse Rate	100	96	116	138
Blood-pressure	46	54	48	45

In this experiment 0.3 c.c. F. E. Squill, U. S. P., 1890, was injected at 10.45 A.M. into the femoral vein of an anæsthetized dog. Then at 2.41 P.M., when the effect of the first injection had passed, the same amount of F. E. Squill, U. S. P., 1900, was injected.

In the second experiment the order of injection was reversed another dog being used for the test, and the same amount of each preparation injected.

EXPERIMENT II.

	F. E. Squill, U. S. P., 1900. Before.	After.	F. E. Squill, U. S. P., 1890. Before.	After.
Pulse Rate	102	144	100	94
Blood-pressure	47	46	52	50

NOTE.—In both cases the U. S. P., 1900, preparatiôn increased the rate and lowered the pressure. This is directly opposite in effect from the characteristic action of the heart tonics in general and from that of the F. E. Squill, U. S. P., 1890, from the same drug.

In this case again a stronger alcohol is better. If the drug is finely ground and extracted with menstrua containing 60 per cent. or less of alcohol, it swells so that percolation is either entirely or almost prevented. It becomes necessary either to cut the bulb without grinding or to mix with sawdust in order to have it sufficiently open to percolate properly. An additional objection is in the large amount of gummy, water-soluble extractive obtained with such menstrua. A fluid extract of better appearance, better keeping quality and containing practically all the available activity of the drug, can be obtained by the use of 80 per cent. alcohol. Repeated experiments have shown the excellence of this menstruum over that of the 7th or 8th Revisions of the U. S. P.

III. Fluid Extract Convallaria, U. S. P., 1900, is not so open to criticism as the others but the menstruum is not entirely satisfactory. There are certain advantages to be gained by using a stronger alcoholic menstruum than that prescribed in the 8th Revision U. S. P. While these advantages are more apparent when experiments are conducted on a manufacturing scale than when small experimental lots of fluid extract are prepared, even in the latter case the advantages are very real.

Several experiments have been carried out, of which the following is used as an example:

A small lot of drug was divided into two portions, one of which was extracted as prescribed in the U. S. P.; namely, with 62.7 per cent. alcohol, the other with 80 per cent. alcohol. These extracts were carefully concentrated to fluid extract volume and tested for activity by the method previously cited, with the following results:

Menstruum.	Per cent. Activity.
62 per cent. alcohol	100
80 per cent. alcohol	120

The advantages to be gained from using a stronger alcoholic menstruum for extracting convallaria roots and rhizome are not merely the greater activity obtainable, but in the improved appearance of the extract and its greater stability. It contains less of the gummy extractives and more alcohol, both of which are desirable features, as they affect deterioration, while the 20 per cent. increase in activity from the use of 80 per cent. alcohol is no less desirable.

It is to be hoped that those in charge of revising the forthcoming U. S. Pharmacopœia will consider these suggestions.

LITERATURE CITED.

[1] AMERICAN JOURNAL OF PHARMACY, October, 1909.
[2] *Jour. American Medical Ass'n.*, June 12, 1906.
[3] *Ibid.*, September 11, 1897.
[4] *Ibid.*, May 12, 1906.

From the Research Laboratory of PARKE, DAVIS & CO.,
Detroit, Michigan.

THE PHYSIOLOGICAL STANDARDIZATION OF THE HEART TONICS.*

BY PROFESSOR WILLIAM A. PEARSON, of The Hahnemann Medical College of Philadelphia.

"The Physiological Testing of the Heart Tonics," which is the subject assigned for my discussion, is a very inaccurate title.

A satisfactory definition of a tonic has never been given, much less, a heart tonic. The word physiological is not appropriate because when any active drug is given the normal processes of the body are no longer physiological.

For these reasons, such a subject as "The Pharmacologic Standardization of Drugs Having a Particular Action on the Heart" would be far more fitting.

Since Digitalis is the most important member of the group of drugs known as "heart tonics," a discussion of the methods of standardizing this drug will be first considered.

MEDICINAL USE AND THERAPEUTIC ACTION OF DIGITALIS.

It is well known that Digitalis has had a place in domestic and medicinal therapy for centuries, and many of you know that a Bir-

* A special lecture given at The Philadelphia College of Pharmacy, December 8, 1913.

mingham physician by the name of Withering,[1] published in 1785 the first reliable observations of the medicinal properties of this drug. The diuretic properties of Digitalis were first observed, but after the middle of the last century its ability to slow the heart so impressed the medical profession that Digitalis was, and is even to this day, often used indiscriminately for all conditions where the heart beat is irregular or rapid. It can now be demonstrated that Digitalis is only of particular value in a very limited number of diseases of the heart and mainly in auricular fibrillation.

So far as showing the rate of the heart beats is concerned, it may be laid down as a law, that Digitalis is far less effective when the rhythm of the heart is normal than when there is auricular fibrillation.[2] Most authors state that digitalis causes constriction of the blood-vessels and consequently a rise in blood-pressure, yet I have not been able to demonstrate more than slight variations in blood-pressure in test animals, although various lots of tinctures, fluid extracts and proprietary preparations have been tried.

Mackenzie [3] has made numerous observations on various classes of patients and refutes the idea that the administration of Digitalis has a tendency to produce fatal syncope, provided the drug is stopped as soon as nausea and vomiting appear or when the heart rate falls below 50 per minute.

When the rhythm of the heart is normal the first symptom is loss of appetite, if drug is continued, vomiting, feeling of malaise, headache, and very little diarrhœa may be reported.

Famulener and Lyons [5] state that the digitalis glucosides act not only on the heart but directly on the central nervous system, first stimulating then depressing it. Cushny [6] states that " the chief therapeutic use is to counteract certain changes in the circulation, which result in the blood accumulating in the veins in too large quantities while the arteries are less filled than usual. In cases of dilation of the heart with a weak and insufficient systole, its action is almost specific.

" In these cases the action is very simple—the increased ventricular systole approaches the normal, the output of the heart is increased, and in some cases the dilation is diminished by the direct action of the drug. The effect is an increased velocity and pressure in the arteries and improved nutrition of the whole body."

There is no doubt that Digitalis relieves distress and dropsy and has been directly responsible for numerous cures, yet it is possible

that these favorable results may be attributed to some other reason than its effect on the heart, *per se*.

It is needless to say that Digitalis has been given thousands of times when its use was not indicated and doubtless its failure to produce favorable results under improper conditions has been responsible, more than once, for condemnation of the particular preparation of digitalis being used.[4] It has been repeatedly stated that analogous preparations of digitalis made by various manufacturers differ markedly in strength, that digitalis preparations rapidly deteriorate and that only the leaves of the first year's plant are active. It is no doubt true that analogous digitalis preparations differ markedly in strength,[7] but it is very doubtful if the usual galenical preparations deteriorate rapidly,[8] or that only the leaves of the first year's plant are active.[9]

It is possible, but not at all probable, that only the digitalis plants which are in flower are physiologically active and this need not exclude the first year's plants as John A. Bornemann[10] has shown me a digitalis plant with plenty of flowers on it, although it was a plant of the first year's growth. Certain it is that the therapeutic action of digitalis as stated by various authors is sadly confusing and no doubt much of this confusion is due not alone to clinical reports where digitalis was not indicated, but to the pharmacologic variability of the preparations themselves.

Chemistry of Digitalis.

Almost every pharmaceutical chemist of note has tried to isolate, unchanged, the complex active principles that are present in digitalis. The great Schmiedeberg and Kiliani agreed that the four glucosides which they separated and called digitoxin, digitalin, digitalein and digitophyllin, possess a true digitalis action. They separated, in addition, other glucosides such as digitonin, digitin and digitoflavin, but they considered these decomposition products. Several carbohydrates which came from the decomposition of the glucosides, were also described.

When one looks up the vast literature on the chemistry of digitalis it is quite evident that different glucosides are sometimes given the same name by different authors and *vice versa*.

Recently Kraft[11] has contributed an admirable article on this subject and his work is now generally accepted. He claims that both Schmiedeberg and Kiliani worked with German digatalin, a commercial product made largely from digitalis seeds, hence their results are

not reliable for digitalis leaves. Kraft has isolated a new active glucoside which he calls Gitalin, which probably has the chemical formula $C_{28}H_{48}O_{10}$. This glucoside is amorphous but forms a crystalline hydrate, $C_{28}H_{48}O_{10}4H_2O$. Gitalin readily decomposes in any solvent except chloroform into anhydrogitalin $C_{23}H_{46}O_9$ which on hydrolysis, with a dilute acid in the presence of alcohol, changes to anhydrogitaligenin $C_{22}H_{34}O_5$ and a sugar which was found to be identical with Kiliani's digitoxose. Another new glucoside was also isolated. This he called Gitin, and it is inactive physiologically. It is crystalline and melts at 265° C. It is considered similar to, but not identical with, Kiliani's digitonin.

Digitoxin is often considered the chief active glucoside in digitalis and chemical determinations of this constituent have been frequently made in the hope of finding a relationship between the digitoxin content and the therapeutic activity, but the results in almost every case have proved a failure.[12] If the digitoxin from a given amount of drug is isolated it will be found that the total amount of digitoxin is very much less toxic than the amount of drug from which it was obtained, hence it seems absolutely necessary to resort to pharmacological standardization if any definite idea of the therapeutic strength is desired.

Pharmacologic Standardization of Digitalis.

At least three distinctly different pharmacologic methods have been proposed for the standardization of Digitalis—the frog method, the guinea pig method, and the cat method.

The Frog Method.

The frog method was first proposed by Houghton in 1898.[13] He found that " fairly accurate data could be obtained from the application of a solution containing Strophanthin, Digitalin, etc., to the laid-bare frog's heart, by comparing the action of the drug thus tested with that of a sample of known strength." After much experimental work this method was replaced by the use of a simpler one—namely, the determination of the minimum lethal dose for frogs under definite conditions. Although the original method as modified by Houghton gives quite satisfactory results, yet various workers have proposed certain changes in the conditions under which the test is to be made. For example, twelve hours was specified as being the length of time that observations should be made after injection of the

frogs. As this is usually inconvenient, these observations were made after one hour, two hours, six hours, or twenty-four hours. Some workers began to pith the frog at the end of one hour and make a direct examination of the condition of the heart, for it was found that sometimes frogs would be apparently normal yet their hearts had been stopped by the drug.

Dr. Hale [14] observed that more concordant results were obtained when the frogs were kept at the uniform temperature of 22° C. It would neither be interesting nor instructive to relate the various modifications that have been proposed for the Houghton method.

Edmunds and Hale,[15] Edmunds and Cushny,[16] and Focke [17] have specified various conditions under which the "frog test" is to be made, but none of these methods make any provision to ***standardize the frogs that are used.***

It is known that variety, weight, sex, season, and temperature affect the resistance of frogs and hence it is possible to obtain different results with different lots of frogs. In order to eliminate these factors of unknown significance in any particular case, Houghton and Hamilton have suggested that a standard be used in testing the resistance of every lot of frogs, at the time the test is made. Upon these data "The Heart Tonic Unit" [18] is computed in every case.

The standard they propose to use is crystalline Strophanthin which is prepared from an authentic specimen of the official drug, *Strophanthus Kombé,* and has been studied in detail by Braun and Closson.[19] The outline of the present method as modified by Houghton is as follows:

Frogs should all be of same species, a convenient variety is the *Rana Pipiens.* They should all be of weights between 15 and 35 gm. and the weights should not vary more than 25 per cent. in any one assay. Before being used the frogs may be kept in any convenient place where the water can be frequently changed and kept at a temperature of about 22° C. During the test the frogs can advantageously be kept in wire cages with sheet iron bottoms, standing in trays of running water, but the depth of water in the cages should not exceed one-half an inch. Scales for weighing the frogs should be accurate within 0.5 gm. The necessary apparatus consists of volumetric flasks, cylinders, graduated pipettes and a 1 c.c. pipette graduated in hundredths of a cubic centimetre and fitted with a hypodermic needle or drawn out into a fine point for injecting.

The solution to be injected should not contain more than 10 per cent. alcohol and the dilution should be made with physiological salt solution (0.85 per cent. NaCl).

The doses are calculated on the weight of the frog, *i.e.*, the M. L. D. is the minimum lethal dose, per gram weight of frog. For example, when the frogs are of average resistance the M. L. D. of Strophanthin is 0.000,001 gm. per gram weight of frog, *i.e.*, for a 30 gram frog the lethal dose of Strophanthin is .000,03 gm., which should be so diluted that this amount is contained in approximately 0.5 c.c. Several series of tests are necessary to establish the activity of any sample of unknown strength and since the frogs vary in resistance among themselves and also because of conditions more or less beyond control, the standard Strophanthin must be tested at the same time. When the M. L. D. of sample and of standard are obtained the activity can readily be expressed in Heart Tonic Units (H. T. U.) by reference to a table.

In the method just given the observations are to be made at the end of twenty-four hours, hence the one-hour method has certain advantages when several series are desired on a single sample as soon as possible. When the one-hour method is used it is necessary to not consider all frogs that have not absorbed the dose injected.

The One-Hour Method.

"In this method the frogs are secured and kept in the manner already described, weighed, and such a dose is injected that the heart will be found in complete systolic contraction at the end of exactly sixty minutes. The drug, properly diluted so as to make a volume of 0.5 to 1 c.c., is injected into the anterior lymph sac by means of a glass pipette. Shortly before the hour is up the frog is pithed, tied to a frog board, and the heart is exposed in the usual manner. If the heart is still beating, the dose has been too small and must be increased in subsequent trials. In the first series doses are chosen with wide limits, which in a second and third series of animals are narrowed down until the smallest amount of the drug which will produce systolic standstill in one hour is found. Usually three series of frogs are sufficient to assay one preparation, but in case of any irregularity in the reaction of any of the frogs a fourth or even a fifth series may be necessary."

The method of Focke [17] is long and complicated and does not appear to have any advantage over the other frog methods that have been described.

GUINEA PIG METHOD.

Reed and Vanderkleed [20] first advocated the advantages of using the guinea pig as the test animal although Houghton [13] had previously tried pigs but considered the frog test more reliable.

The closer biologic relation of the guinea pig to man appears to be one important reason for preferring guinea pigs. It is claimed [21] that "frogs not only show the pharmacological action of the drug under test, but they react with so near an approach to uniformity that the medicinal value of a tested specimen can be gauged by the determination of the minimum fatal dose—for the slowing of the heart beat and the systolic emphasis produced by active heart tonics are directly proportioned to the quantity of the drug administered, and under progressive doses at last reach a point which is incompatible with life."

DETAILS OF REED AND VANDERKLEED METHOD FOR TESTING DIGITALIS AND ITS PREPARATIONS.

If Digitalis leaves are to be tested a tincture is first prepared from the sample by the U. S. P. process.

An amount of any alcoholic preparation representing one-tenth of a gramme of Digitalis Leaves is placed in a very small watch glass and the excess of alcohol evaporated from it at room temperature by placing the vessel in a current of air. This residue is then carefully washed into a Hitchen's syringe [22] with sufficient physiological salt solution to make the total volume two cubic centimetres.

The hypodermatic needle is previously sealed with sufficient petrolatum to prevent loss of this solution.

Two cubic centimetres of physiological salt solution is placed in the side-arm of the syringe and the needle inserted under the skin of a guinea pig weighing about 250 gm.

The solution of the drug is then injected and the last portions washed under the skin with the physiological salt solution which was placed in the side arm, without removing the needle.

Great precaution is taken to inject accurate amounts and always a total of four cubic centimetres of liquid (2 c.c. of solution of drug and 2 c.c. of physiological salt).

After the injection, the guinea pig is kept under close observation and evidences and time of salivation, purgation and convulsions noted. If the pig should not develop these symptoms and die within two hours, another pig is injected with a larger quantity of the drug.

The tests are repeated until the amount of the drug is found which will produce the characteristic symptoms of Digitalis poisoning and kill a 250 gm. guinea pig in two hours.

Post-mortem examinations are always made to note the condition of the heart and dilation of the blood-vessels.

In testing solid preparations of Digitalis a weighed quantity of the preparation is shaken with a definite amount of physiological salt solution so that two cubic centimetres of the liquid will represent one-tenth gramme of the drug. This method has been found quite satisfactory, but Pittinger [23] has found that more concordant results are obtained if the time of observation is extended from two hours to twenty-four hours. One disadvantage to the method is that the cost of the required pigs is usually greater than the frogs necessary for Houghton's method. This objection is largely overcome by manufacturers of antitoxin who can use the pigs that have survived the antitoxin tests for digitalis tests. These pigs cannot again be used for testing serum on account of anaphylaxis, and by the time they have completely recovered from the antitoxin tests they may weigh much more than 250 gm., which is the weight specified. No provision is made for the varying susceptibility of the pigs and it is doubtful if the pig test, as it is usually carried out, will give any more reliable results than a larger number of frogs that have been " standardized " with crystalline strophanthin.

The Cat Method of Hatcher and Brodie.[24]

This method is based upon the determination of the minimum lethal dose for cats. The cat is anæsthetized with ether and about one-half of the amount of the preparation being tested necessary to kill the animal is injected directly into the venous circulation. The originators of this test have found that if preparations of digitalis or other members of this series are injected until the cat dies, the results will usually be too high, hence, after twenty minutes a 1 to 100,000 solution of Merck's Ouabain is cautiously injected until the cat shows signs of dying, namely, rapid respiration, which soon becomes irregular and is accompanied by convulsive movements. The Ouabain should be injected in such amounts that the cat should die ninety minutes after the beginning of the test.

The " cat unit " is the amount of crystalline Merck's Ouabain which is fatal within about ninety minutes to each kilogram body

weight of the cat. This amounts to 0.1 milligramme of the Ouabain and the number of "cat units" in one cubic centimetre of the preparation being tested is computed from the data obtained. Eckler [25] has reported serious disadvantages to this method, and it is doubtful if it will ever have the popular favor the other two methods enjoy.

Factors Relating to the Standardization of Digitalis.

It may easily be seen that the last word has not been said in regard to the standardization of Digitalis and this unsettled condition, in its standardization, is certain to prevail until the therapeutic uses and chemistry of the drug are agreed upon.

It is true that some fault can be found with the methods we have outlined and no doubt many factors will soon be eliminated.

At the present time, it is possible to determine by physiological tests with reasonable accuracy the variability of the crude drug, the stability of its preparations, and to prepare preparations of considerable uniformity.[26]

Other Heart Tonics.

What has been said in regard to the methods used for standardizing Digitalis applies also to preparations of Strophanthus, Squill and Convallaria. Strophanthus seems to be more certain in its action than digitalis and can also be advantageously tested by the blood-pressure method upon dogs.

Cactus grandiflorus has long been used empirically with apparently favorable results, yet competent pharmacologists have reported that it has no action analogous to digitalis [27,28]. Graeber [29] has recently reported the presence of both alkaloids and glucosides in this drug and publishes experiments on frogs which "indicate that *Cactus grandiflorus* actually is possessed of an action upon the heart such as belongs to the substances of the digitalis group." In all his frog experiments the frequency of the pulse was reduced and the systole strengthened.

Sparteine sulphate is considered a drug of mediocre importance as a "heart tonic," yet Pettey [30] considers that Sparteine is unappreciated because it is not given in sufficient doses. He recommends the use of 2 grain doses as a true and reliable heart tonic, an excellent non-irritating diuretic and states that this dose is entirely free from untoward or objectionable effects.

Work of the Normal Heart.

Few realize the vast amount of work performed each day by the heart of the normal adult. One-fifth the total muscular energy of the body is used in propelling the heart and about twelve tons of blood are pumped each day.

New Methods of Observing Conditions of the Heart.

The electro-cardiographic method [31] has made possible not only the accurate diagnosis of diseases of the heart but also enables the physician to observe the effects of the medicine he has prescribed. The practice of medicine under these conditions has become scientific, not empiric, and if uniform preparations of the "heart tonics" can be supplied, the physician needs only to consider the idiosyncrasy of the patient.

Summary.

In presenting this subject I have attempted to dwell not alone on the methods used in standardizing the "heart tonics" but the various factors that must be considered in producing reliable and potent preparations. The clinical side of the problem must not be lost sight of, and when a preparation is made that will produce certain therapeutic results it is of vital importance to produce another lot having the same action. Uniformity is practically as important as potency. When a competent observer like Faught [32] says "Usual preparations are variable and cannot be depended upon unless coming from a reliable source. I have seen less effect follow the administration of 20 minims of a poor preparation than 5 minims of a good active one" it is time to improve conditions. Conditions can be improved by the adoption of pharmacological standards and methods for these drugs. At the present time the manufacturers who have wisely adopted physiological standardization of their products often have different standards while those that have not adopted physiological standards have no assurity that these important drugs are even active.

BIBLIOGRAPHY.

[1] Withering, "An Account of the Foxglove and Some of its Medicinal Uses."
[2] Mackenzie, "Digitalis" Heart, volume 2, No. 4, page 279.
[3] Mackenzie, "A Scheme for Investigating the Treatment on the Human Heart" Heart, volume 2, page 9.
[4] Berkeley, Merck's Archives, September, 1910, page 275.
[5] Proceedings of American Pharmaceutical Association, 1902, page 415.
[6] Cushny, "Pharmacology and Therapeutics."

[7] *Journal of Amer. Med. Assoc.*, September 13, 1913.
[8] "Observations on the Keeping Properties of Digitalis and Some of Its Preparations," Hatcher and Eggleston. AMERICAN JOURNAL OF PHARMACY, 1913, page 203.
[9] Miller and Baker, 8th International Congress of Applied Chemistry.
[10] Personal Communication.
[11] Kraft, *Arch. der Pharm.*, 1912.
[12] Edmunds and Hale, "The Physiological Standardization of Digitalis."
[13] Houghton, *Journal of American Medical Association*, June 7–10, 1898.
[14] Hale, The Physiological Standardization of Drugs, AMERICAN JOURNAL OF PHARMACY, 1911.
[15] United States Hygienic Laboratory, Bulletin 48.
[16] "Laboratory Guide in Experimental Pharmacology," Geo. Wahr, publisher.
[17] Focke, *Arch. d. Pharm.*, 1903, 241, page 678.
[18] Hamilton, "The Heart Tonic Unit," AMERICAN JOURNAL OF PHARMACY, 1912, page 97.
[19] Braun and Closson, "The Chemical Constitution of Crystalline Strophanthus," *Jour. of Amer. Pharm. Assoc.*, 1913.
[20] Reed and Vanderkled, AMERICAN JOURNAL OF PHARMACY, 1908, page 110.
[21] "Standardization of Pharmaceutical and Biological Products," Parke, Davis and Co.
[22] Hitchens. *Journal of Experimental Medicine*, 1905.
[23] Pittinger, 1912 Proceedings American Therapeutic Society.
[24] Hatcher and Brodie, AMERICAN JOURNAL OF PHARMACY, 1910, page 362.
[25] Eckler, AMERICAN JOURNAL OF PHARMACY, October, 1911.
[26] Hale, Factors Relating to the Standardization of Digitalis; Proceedings of American Pharmaceutical Association, 1909.
[27] Hatcher and Bailey, *Jour. Amer. Med. Assoc.*, 1907, page 1021.
[28] Lyon and Quall, *Jour. Amer. Med. Assoc.*, 1910, pages 455, 459, 508.
[29] Graeber, *Therapeutische Monatshefte*, 1913, page 581.
[30] Pettey, "The Therapeutic Virtues of Sparetine Sulphate." *Clinical Medicine*, Sept., 1913.
[31] Lewis, "Clinical Electrocardiography."
[32] Faught, "Blood-Pressure from Clinical Standpoint," page 268.

COLLOIDS AND CRYSTALS, THE TWO WORLDS OF MATTER.*

BY ROBERT H. BRADBURY,

Head of the Department of Science in the Southern High School, Philadelphia.

When a solid is brought into contact with a liquid the result depends upon the nature of both. There may be apparently an entire

---

* Presented at the meeting of the Section of Physics and Chemistry held Thursday, April 10, 1913, and reprinted from *Jour. Franklin Institute*, September, 1913.

absence of interaction, as when rosin is shaken up with water or chalk with alcohol. Or, as when sugar is agitated with water, the solid may disappear, entering into solution in the liquid. The study of sugar solution shows quite clearly that the connection of the sugar molecules with each other has been completely destroyed. They are dispersed through the water very much as the molecules of a gas distribute themselves uniformly in a vacant space, and in both cases the permanence of the uniform dispersion is due to the incessant motion of the molecules. Were the molecules at rest, both the sugar and the gas would settle and form a layer on the bottom of the containing vessel.

However, the molecules of the sugar retain their structure intact, the action being limited to their dispersion. When salt, on the other hand, is dissolved in water, a further breakdown occurs, the molecule is separated and ions of sodium and of chlorine move about in the liquid. Both solutions freeze below 0° C. and boil above 100° C. The most important difference between them is that the salt solution conducts the electric current, while the sugar solution is as poor a conductor as water itself.

A fourth possibility presents itself when glue or gelatin is treated with water. The gelatin absorbs water, swells up and, under the influence of heat, dissolves, but the liquid freezes and boils at practically the same temperatures as pure water. The study of the solution shows that the dispersion is not molecular. The particles of gelatin in it are composed of variable and rather large numbers of molecules. A system like this gelatin solution which presents a case of very fine but not molecular subdivision is called a *colloidal solution.* There are certain solids such as gelatin and dextrin (with water), and rubber (with benzene and carbon disulphide), which, when they dissolve in liquids, are invariably dispersed in this way. Such solids may properly be referred to as *colloids.* They are all amorphous. Crystallized substances never yield colloidal solutions by mere spontaneous solution in a liquid. They always produce molecular or ionic dispersions. However, the phenomenon of colloidal solution is perfectly general, and crystallized substances can also be obtained in this condition, but not by mere solution.

It is an interesting fact that a substance which yields a colloidal solution with one solvent may form an ordinary molecular solution with another. Soap is an example. Its concentrated solution in

water boils at about 100°, freezes at about 0°, and exhibits the behavior of a colloidal solution in general. On the contrary, a soap solution in alcohol shows the normal change in freezing and boiling points corresponding to the molecular weight, and conducts itself in all respects like an ordinary molecular dispersion.

II.

Every one is familiar with the distinctions between solutions and suspensions. Suspensions are turbid in aspect, and the solid can be removed by letting it settle, or by filtration. Solutions are clear, dissolved matter does not subside and is unaffected by filtering. Colloidal solutions occupy an intermediate position.

Consider for a moment the effect of increasing subdivision on a suspension of finely-divided gold in water. So long as the diameter of the particles is much greater than a thousandth of a millimetre,[1] the system will be turbid and the gold will settle rapidly. But the wave-length of visible light ranges between 0.4 μ and 0.7 μ, and when the particles become smaller than this they can no longer reflect light and the liquid will appear clear. At the same time there will be a rapid falling off in the speed of settling. Stokes has derived a formula for the velocity of subsidence, V, of small spheres of radius R and density S falling in a liquid of density S' and internal friction f under the force of gravity g:

$$V = \frac{2}{9} g (S - S') \frac{R^2}{f}$$

Substituting the proper values for gold and water and assuming a radius of μ for the particles, the value for V is about 14 centimetres per hour. This means, of course, that the system would be a coarse suspension and would clear up at once. But when $R = 10\ \mu\mu$, V is only about a centimetre a month. This begins already to be fairly permanent. It must be remembered that the high density of gold (19.5) increases the rapidity of subsidence. If we make the calculation for $S = 3$, which is about the density of arsenious sulphide, V comes out only about a millimetre a month.

---

[1] It is usual to employ the symbol μ (the Greek letter mu) for the thousandth of a millimetre. In the same way $\mu\ \mu$ indicates the millionth of a millimetre.

So much for calculation. Now what are the facts? As a matter of fact, the dispersed substance in a colloidal solution does not settle at all, so long as the subdivision is maintained. Colloidal gold solutions have been preserved unchanged for years. I have a solution of arsenious sulphide which has remained apparently unchanged for three years and whose countless particles can readily be seen, engaged in their incessant Brownian movement, with an ordinary oil immersion lens. Whenever settling does occur, it is preceded by the aggregation of the particles into larger particles, which finally attain a diameter of μ or over, and slowly subside.

Here, then, is an apparent discrepancy between Stokes' law and the facts. The law informs us that the speed of subsidence decreases rapidly with decreasing radius of the particles, but it does not lead us to expect the total absence of settling which presents itself when the average radius is 10 $\mu\mu$ or thereabout.

The explanation, of course, is molecular motion, or, in other words, *heat*. The particles are battered, on all sides, by a hail-storm of molecular impacts. If the particle is large, the blows of the molecules of the solvent in different directions neutralize each other. But when the particle is not so very much larger than the molecules themselves a molecule striking, say on the left, will give the particle a very perceptible push toward the right, "just as a cork follows better than a large ship the motion of the waves of the sea."[2] As the dimensions of the particle approach the molecular dimensions it begins to behave like a molecule and is swept along in the endless molecular movement. The cause which prevents the particles in a colloidal solution from settling is in no way different from the cause which prevents the earth's atmosphere from subsiding to a snowy layer a few feet deep on the surface of the planet.

It is worth remembering, also, that the particles of the dispersed phase ordinarily possess an electric charge, which is usually negative. The effect of the repulsion of these similar charges would be to preserve the distribution of the particles throughout the liquid. It is a fact that, when the charges are removed, the system becomes instable and subsidence—preceded by coalescence of the small particles—readily, but not necessarily, occurs.

---

[2] Perrin.

III.

On the subject of the classification of colloid systems we must be very brief. One proposal subdivides them into *suspensoids,* such as the sols [3] of gold and arsenious sulphide, in which the dispersed phase is solid, and *emulsoids,* in which the dispersed phase is liquid. This classification would appear to be an attempt to extend the familiar distinction between liquid and solid to a domain in which that distinction has little if any meaning. To assert that a thing is solid is to say that it has a definite shape, which it retains with some persistence. There is not the slightest reason to think that the particles in a gold sol are solid. It is usual to assume that they are spherical, but this is done merely because it is the simplest assumption to make. There are faint indications that they really have the form of leaflets or of little rods, but they appear in the ultra-microscope simply as brilliant dancing points, and in reality we know nothing whatever about their shape. In connection with this it is interesting to recall the fact that the formation of a crystal begins with the appearance of minute liquid spheres (globulites),[4] which pass through several stages (margarites, longulites, etc.) before the crystal is formed. It seems possible that, under such enormous subdivision, cohesion retires into the background and surface tension assumes the chief rôle, so that the gold particles are rather to be compared to minute drops than to little crystals.

Enough has been said to make clear the uncertainty which attaches to the attempt to classify colloid solutions according to the state of aggregation of the particles. A better classification is into *reversible* and *irreversible* colloids, according to the way in which the dissolved substance behaves when separated from the solution. Thus, when a gelatin solution is evaporated until it "sets" it is only necessary to warm the jelly with water to obtain it again in colloid solution. Gelatin is a typical reversible colloid. But when the gold is caused to separate from a gold sol—which can easily be brought about by adding any electrolyte to the sol—the gold will not again enter into colloidal solution. Shaking or warming with water gives a mere

[3] Thomas Graham introduced the term sol as an abbreviation for colloidal solution.

[4] Fink, "Poggendorff's Annalen," vol. 46, p. 258 (1839); Schmidt, "Liebig's Annalen der Chemie," vol. 53, p. 171 (1845); Frankenheim, "Poggendorff's Annalen," vol. 111, p. 1 (1860).

suspension, which settles at once. Gold is an *irreversible* colloid. The distinction is fundamental. Many organic colloids are reversible, while it is rather the habit of the inorganic colloids to behave in the irreversible way.

IV.

In order to prepare a sol containing an irreversible colloid all that is necessary is to reduce the solid to extreme subdivision in a liquid in which it is insoluble. The electric arc furnishes a rapid and simple method.[5] Two gold wires about 2 mm. thick are connected with a 220-volt circuit and brought together under distilled water. A 110-volt circuit can be used, but more patience is required. Sols of platinum, silver, copper, and other metals can be made in the same way. By related electrical methods, using such liquids as pentane and anhydrous ether, Svedberg[6] obtained sols of all five of the alkali metals. The colors of the sols agreed with those of the vapors of the corresponding metals.

Chemical reduction of a salt of a metal furnishes another method which has been largely employed by Zsigmondy[7] and other investigators. For instance, a very dilute solution of auric chloride is mixed with such reducing agents as formaldehyde, hydroxylamine or an ethereal solution of phosphorus. The gold sols obtained in this way are usually red by transmitted light, the particles being bright green and very much smaller than in the sols obtained by the electrical method.

By various chemical methods, which lack of space forbids us to discuss, sols of sulphides (CdS, As_2S_3, Sb_2S_3, etc.) and oxides (Fe_2O_3, Al_2O_3) can be obtained. The sol of aluminum oxide is important on account of its connection with dyeing and mordanting. The formation of the blood-red sol of ferric oxide by adding a concentrated solution of ferric chloride to about 50 volumes of boiling distilled water is a simple and beautiful lecture experiment.

In making colloidal solutions of *salts,* the essential thing is to mix dilute solutions of the precipitants, using a liquid in which the

---

[5] Bredig, *Zeitschrift für angewandte Chemie,* 1898, p. 951. For a full account of Bredig's work with the platinum sol see *Zeitschrift für physikalische Chemie,* vol. 31, pp. 258–353 (1899).

[6] *Berichte der deutschen chemischen Gesellschaft,* vol. 38, p. 3616 (1905).

[7] See his monograph, "Zur Erkentniss der Kolloide" (Jena, 1905), which has been translated by Jerome Alexander.

insolubility of the product is as complete as possible. Thus, in mixing very dilute solutions of sodium sulphate and barium chloride, a crystalline precipitate is usually obtained. The reason is that barium sulphate possesses a very slight but real solubility in water. Hence the liquid in contact with the particles first formed contains enough barium sulphate to nourish their growth and allow them to develop to crystals. If alcohol is added to the sulphate, before the barium chloride is introduced, the solubility of the barium sulphate is greatly reduced, and it is obtained in colloidal solution without difficulty.

In the same way, if we mix water solutions of sodium hydroxide and of hydrochloric acid we obtain merely an ordinary solution of common salt. But if salt is produced by a reaction between organic compounds in a liquid in which the sodium chloride is insoluble, then a colloidal solution is obtained. For instance, when chlor-acetic ester interacts with sodio-malonic ester a grayish opalescent sol of sodium chloride in ethenyl tri-carboxylic ester results: $CH_2Cl\ COOC_2H_5 + CHNa(COOC_2H_5)_2 = CH_2(COOC_2H_5) - CH(COOC_2H_5)_2 + NaCl$. At low temperatures, in such liquids as toluene and chloroform, even *ice* has been obtained in colloidal solution.

V.

The most striking property of the reversible colloids is that they are able to communicate their reversibility to the irreversible ones. Thus, if a trace of gelatin is added to a gold solution, the gold becomes much more difficult to coagulate by electrolytes, and when coagulated it can be dispersed again by merely warming with water. This curious protective action is exerted, in greatly varying degree, by most reversible colloids. Direct study of the phenomenon with the ultra-microscope shows that the view frequently expressed that the gelatin envelops or forms a film around the gold particles is incorrect. What actually happens seems to be a direct combination between gelatin particles and gold particles, which then pass through the reversible changes together.

Protective colloids enjoy a wide practical application. In the manufacture of photographic films the gelatin retards the crystallization of the silver bromide. Ink often contains a colloid which prevents the pigment from settling. The lubricant "aqua dag" put in the market by the Acheson Company consists of finely-divided artificial graphite, held up by a protective colloid. Clay is made plastic

for the potter by an empirical process which involves the action of protective colloids derived from decaying vegetable matter. The addition of gelatin in making ice cream depends upon its protective action in preventing the growth of ice crystals, which would make the product "gritty." Without doubt protective action plays an important rôle in the cleansing action of soap. This has been made clear by some recent experiments of Spring.[8] Lampblack, freed from oil by long washing with alcohol, ether, and benzene, forms a rather stable suspension in water, but the lampblack is detained by a paper filter. If the filter is now reversed, so that the blackened surface is outward, and water poured through it, the lampblack is not removed, but a dilute soap solution removes the coating and cleanses the filter at once. Finally, lampblack suspended—or colloidally dissolved—in soap solution, passes through a filter unchanged. It is of much practical interest that there is a well-marked optimum in the concentration of the soap required to protect the lampblack. A one per cent. soap solution is the most efficient. In two per cent. soap solution lampblack sinks about as rapidly as in pure water.

VI.

We have already considered the probable actual condition of the particles in a colloidal solution and have concluded that, for the present, no very definite information is obtainable about the matter. We must now return, for a moment, to the subject in order to allude to the thesis so brilliantly advocated by van Weimarn, the Russian investigator, who holds that the particles are of necessity minute crystals and that there is, in fact, no such thing as amorphous matter. He even goes so far as to state that substances like air and water are in a "dynamic crypto-crystalline condition," though I have been unable to understand what he means by this statement.

Briefly, the evidence that van Weimarn adduces to the support of his hypothesis is:

(1) That colloid particles will grow to crystals if provided with the proper nourishment, namely, a dilute solution of the same substance.

(2) That colloid particles are capable, when introduced into

---

[8] *Kolloid Zeitschrift*, vol. 4, p. 161 (1909); *Kolloid Zeitschrift*, vol. 6, pp. 11, 109, 164 (1910).

a supersaturated solution of the same substance, of discharging the supersaturation and inducing the formation of crystals.

Those who desire to follow this matter further should read van Weimarn's little book, "Grundzüge der Dispersoidchemie," after which they will find themselves very much interested, but somewhat unconvinced. Let me hasten to add that I have not the least desire to undervalue the brilliant experimental work of the Russian chemist. It is, in fact, precisely by the conception of more or less daring hypotheses, and the working out of their consequences, that our science achieves its endless victory over the nescience about us.

VII.

We have seen that the wave-lengths of the visible radiations are comprised between 0.4 μ and 0.7 μ. With objects much smaller, the ordinary microscopic method ceases to be applicable. Using ultraviolet radiation for illumination, quartz lenses in the microscope, and receiving the image with the photographic plate instead of the eye, it is possible to advance a step further in the domain of the infinitesimal, but only a step, and there are obvious objections to the proceeding. Since some of the particles in colloidal solutions are only 0.006 μ in diameter, we can never hope to see them as little bodies subtending a visual angle. The *ultra-microscope*—the powerful instrument of investigation to which most of our knowledge of colloid systems is due—renounces this idea and makes the particles visible merely as glittering points on a black background. The sol is placed in a small rectangular glass trough and a horizontal beam of arc light or sunlight focussed in it. The microscope is placed vertically above the trough. It will at once be seen that there are two fundamental things about the instrument: to provide intense illumination, and to make sure that no light enters the microscope except the rays which emanate from the particles. The principle is simple, but the system of diaphragms and lenses needed to secure the second object makes the ultra-microscope an elaborate and expensive instrument in practice.

Cotton and Mouton [9] achieve the same end in a different way. The illumination (arc or sunlight) is thrown up from below by a paraboloid reflector so ground that all rays, *except those diffracted*

---

[9] *Compt. Rendus,* vol. 136, p. 1657 (1903).

by the particles, are totally reflected from the cover-glass over the sol. This instrument is simple, easily adjusted and cheap. It is made commercially by the firm of Zeiss. It would seem to be admirably adapted to school purposes. In fact, after a look into the ultra-microscope, the study of the molecular topics ceases to be drudgery and becomes a positive intellectual need.

VIII.

Even a brief glance at the subject of colloid systems must at least mention the classic work of Perrin [10] on the distribution of the particles in suspensions of gamboge and mastic. He succeeded, by an ingenious and simple method, in preparing emulsions of gamboge in water in which the spherical yellow granules were all of the same diameter. If we consider a mass of such a liquid in a tube, it is clear that the granules, if at rest, would, since they are denser than water, all fall to the bottom. The fact that they remain suspended is due to their movement. In other words, the state of things is the same as in the earth's atmosphere, and just as the molecules are more crowded near the earth's surface, so the granules of gamboge must be more numerous near the bottom of the liquid than in the upper layers. Perrin verified this prediction by direct counting of the granules under the microscope. The barometric formula which describes the progressive rarefaction of air with increasing height also describes the distribution of the granules in Perrin's uniform emulsions. The only difference is that, while the aviator must ascend six kilometres in order to reach air half as dense as at sea level, the same effect is produced, in Perrin's emulsion, by an ascent of 0.1 millimetre.

That the mean energy of rotation of a molecule must be equal to its mean energy of translation is one of the chief propositions of the kinetic theory. Perrin has proved this by direct measurement of the rotation of granules under the microscope. For this purpose, large granules (15 μ) of mastic were employed. These are far too heavy to remain suspended in water, so a solution of urea was used. Fortunately, the granules contain little inclusions which make it possible to measure their rotation.

---

[10] *Annales de Chimie et de Physique,* 3d series, vol. 18, p. 5 (1909). There is a German translation by Donau in *Kolloidchemische Beihefte,* vol. 1, p. 1 (1910). An English translation by Soddy has appeared in book form under the title "The Brownian Movement and Molecular Reality."

These are only two of many fundamental results contained in this wonderful memoir. Van't Hoff extended the gas laws to solutions. Perrin has now proved them to be valid for systems in which the moving particles are visible realities. Let us end by quoting one of the sentences of his conclusion:

"La découverte de telles relations marque le point où s'élève, dans notre conscience scientifique, la réalité moléculaire sousjacente."

THE INFLUENCE OF HEAT AND CHEMICALS ON THE STARCH GRAIN.[1]

By Henry Kraemer.

In presenting some of the most recent observations on the starch grain, it may be well to consider for a moment the nature and origin of starch. In a way starch is one of the most remarkable substances produced by the plant. It is the first visible product formed by the chloroplastid, or chlorophyll bodies, from the inorganic substances, carbon dioxide and water. Inasmuch as sunlight seems to be necessary to bring about this transformation the process is looked upon as one which involves the converting of the sun's energy into vital energy.

The substance thus formed by the chloroplastid through the influence of sunlight, in the leaves and other green parts of plants, is known as "assimilation starch," and serves subsequently not only as a food for the plant itself but is also the source of the energy of the animal world. Assimilation starch is not stored in the cells where it is manufactured, but each night through the influence of the plant ferments the starch formed during the day is converted into a soluble form, and transported to various other parts of the plant. In some cases this soluble starch is temporarily stored in the cells of the pith, medullary rays, or bark, and has received the name of "depot starch." While some of the soluble carbohydrate is converted into fixed oils and other substances, a considerable portion of it is carried to some reserve organ, as a root, tuber, rhizome, or seed, and under the influence of a plastid similar to the chloroplastid, converted into a stable form, known as *reserve starch.*

---

[1] Reprinted from Original Communications, Eighth International Congress of Applied Chemistry. Vol. XVII—Page 31.

This is the product with which we are specially concerned in the present article. Heretofore, the minute study of the starch grain, particularly of its structure, has been of scientific interest only, but with the application of scientific methods in nearly every department of industry, it is coming to have a practical application.

The commercial reserve starches are derived from various plants, and not only enter largely into food products but are also used for a variety of technical purposes. The grains of the reserve starches have a number of characteristic features. They vary in size, in shape, in internal structure, and also to a considerable extent in composition. The variation in composition is shown by the use of aniline stain and also by the use of iodine. By the treatment of starch with iodine solution, we may distinguish three kinds of reserve starch: (1) one which is colored deep blue, as potato and maranta; (2) one which is colored somewhat purplish, changing to cinnamon-brown, as corn and wheat; and (3) one which is colored brownish-red, as in the amylo-dextrin starches of comfrey and a few other plants.

The shape of the grains varies from polygonal to ellipsoidal, the shape being influenced by the number of grains in a cell. Under the micro-polariscope the grains are seen to be anisotropic, the polarization effects differing with the grains of the different classes. Polarizing effects are usually produced by crystals, but may be produced by substances in a condition of tension, as minute globules of glass. It should also be stated that cell walls have this same property of double refraction, and it is very likely that the substances in the starch grains, as well as in the cell wall, are crystalloidal and arranged in spherite aggregates, resembling those of inulin, a product closely resembling starch.

The theories which have been advanced regarding the structure of the starch grain, have been largely based on studies of the potato starch grain. It was originally thought to be in the nature of a globule filled with a fluid. Fritzche, Schleiden and others considered it to be made up of more or less concentric layers formed around a central or excentral point. While it may be true, as pointed out by Naegeli, that many of the reserve and glucose starch grains arise free in the cell, the view of Schimper that starch grains always develop within plastids, is generally accepted at the present time.

The internal structure of the starch grain is shown in several

ways. When starch is treated with certain chemicals, or heated with water alone to a temperature of 60° C., the grains show a series of successive changes. First, the lamellæ or layers become more distinct, and the layers appear to be made up of parallel crystal-like particles, these latter being more numerous in successive alternate lamellæ. Then as the grain swells clefts which radiate from the centre are formed. Later the centre of the grain becomes hollow, and when the grain has swollen to about four times its original size the outer membrane breaks and the contents are gradually dissolved.

Some striking effects are also produced when starch is carefully treated with aniline dyes. The point of origin of growth and the successive layers alternating with it take up the stains, thus again showing the distinct character of the two kinds of lamellæ making up the grains. When plant material containing mucilage is treated with aniline stains, the stain is taken up only by the cells containing mucilage, and this indicates that the lamellæ in a starch grain which take up the stains are composed chiefly of colloidal substances. From these observations it is apparent that the grains of certain of the starches, as the potato, if not of all the lamellated starch grains, are made up of two kinds of lamellæ, one rich in colloids and one rich in crystalloids. The presence of two kinds of lamellæ, at least in certain of the starch grains, and their difference of composition are further shown by the use of a weak solution of iodine, the so-called crystalloidal layers or lamellæ taking up the iodine and becoming blue.[2]

Recently I have been conducting some experiments to determine further the effects of heat upon the structure of the starch grain. When starch alone is heated to between 45° and 50° C. from 15 to 30 minutes, the lamellæ and the crystalloidal structure of the grains are brought out. The grain is so resistent that the inner structure does not appear to be lost until a temperature of over 125° C. is attained. Between 140° and 160° C. the polarization effects of the grains become faint, except in the case of potato starch, which now in addition gives chromatic effects. At 240° C. all of the grains are disintegrated except those of corn starch, the individual grains of which are of a brownish-yellow color and not perceptibly

[2] Kraemer, *Bot. Gazette,* Vol. XXXIV, Nov., 1902; *Ibid.,* Vol. XL, Oct., 1905; reprinted in *Amer. Jour. Pharm.,* Vol. 79, 1907, pp. 217–229; 412–418.

swollen. Besides the entire mass is more or less granular, while in the case of the other starches examined the charred mass is in a puffed condition.

The effects produced when starch is heated in the presence of a fixed oil, as almond oil, are of special interest. The inner structure of the starch grain is not usually apparent when it is mounted in a fixed oil, unless the starch has been previously heated to a temperature of from 80° to 160° C. When, however, a mixture of starch and oil is heated as high as 180 C. the grains still polarize light, which shows that the structure has not been altered. In other words the effects of heat on the grain are more or less neutralized by the presence of the oil. On heating the mixture up to 250° C. most of the grains still show their individual character, but no longer polarize light. They are but slightly swollen, and in the case of cassava and corn starch a central differential area occupies from one-half to nine-tenths of the original area of the grain.

It may be worth while to state that when starch and water in the proportion of 2 gm. of the former to 100 c.c. of the latter, are heated together at a temperature of between 90° and 100° C. in a steam sterilizer seven or eight hours a day for a long period, even extending to months, dextrinization of the starch does not take place, that is, the solution still gives a blue color with iodine. Even though the operation be conducted in an autoclave under a pressure of 20 pounds for about ten hours, dextrinization is not effected. If, however, 1 c.c. of N/HCl be added to 100 c.c. of water and this heated for five hours with 1 gm. of starch, the resulting solution is colored red with iodine. When the amount of the acid is reduced to .2 c.c. and the mixture heated under a pressure up to 12 pounds for one hour, cassava, corn, maranta and potato starch solutions give a deep blue color with iodine, while a solution of wheat starch gives a deep purple color with iodine. If the heat be continued an hour longer, wheat starch gives a purplish-red color, cassava a deep wine color, maranta and potato a light purple, while corn still gives a blue reaction with iodine.

These observations may be summarized as follows:

1. The starch grain consists of two nearly related substances: (*a*) a colloidal or mucilage-like substance which takes up aniline

dyes, and (*b*) a crystalloidal or crystal-like material giving a blue color with iodine.

2. The starch grain is made up of concentric layers, one series of which contains a large proportion of crystalloids, while the alternate layers are composed mostly of colloids.

3. The polarization effects produced by starch are probably to be attributed to the crystalloidal character of the grains.

4. The starch grains retain their polarizing properties even when heated up to a temperature of 180° C., which seems very remarkable indeed.

5. At the higher temperatures the potato starch grains give chromatic effects in addition, similar to those when a selenite plate is used.

6. While heating the starch grains in water rapidly changes the structure of the grain, it is only by the addition of chemicals or ferments that dextrinization is brought about.

BOOK REVIEWS.

Semi-Annual Report on Essential Oils, Synthetic Perfumes, &c. Published by Schimmel & Co. (Fritzsche Brothers), Miltitz near Leipzig. London, New York. October, 1913.

In the introduction to this report an admirable résumé is given of conditions, both favorable and adverse, which affected business in the last year and particularly as to commodities handled by this firm.

As is known to well-informed pharmacists, the practice of sophistication is found in many branches of business but in none so much as in the essential oil industry. In fact, one is almost led to believe that adulteration of oils and perfumes is an industry in itself. Upward movement of prices is the dominant cause for this, and, as is always the way, the forces of evil and dishonesty are up and doing, and "the practice of adulteration is assuming dimensions, and is pursued with refinements of ingenuity that baffle description." So cleverly are adulterants selected and manipulated that the constants of an adulterated oil are kept within the right limits of value and only a most thorough examination will show the true state of affairs. Artificial esters play an important part in this nefarious work; for instance, when added to oils such as lavender

and bergamot, they give "to them the appearance of containing far more linalyl acetate than the oils possess in reality."

In this report the statement is made that there are firms who do not hesitate to offer such esters openly for purposes of adulteration. Furthermore, it is stated that one firm made such an offer to the Schimmel people in writing who publish this communication in the original language and a translation of which follows:

GENTLEMEN:

For some years past we have been in the habit of supplying to lavender growers a product called "Ether L."

The advantage of this article is that it simulates in a perfect manner essential oil of lavender, and we have judged it opportune to forward you to-day a sample of it by post. The price is 12.50 francs per kilo delivered at your works.

If this product should interest you by any chance, please let us know what quantities of it you would be able to use annually.

Hoping to hear from you we are, &c.,

N. V. Polak & Schwarz's,
Essence Fabrieken,
Zaandam (Holland).

P. S.—Our Ether L. is pure and contains 100 p. c.

Subsequent examination of this product showed that instead of being 100 per cent. it revealed a percentage of 86. The presence of this ester in lavender oil would not prove difficult of detection.

The high price of menthol also proved a stimulus to those of dishonest tendencies. Two samples examined showed 100 per cent. adulteration. Both were acetanilid, one scented with menthol and the other with peppermint oil. Under the name Mentholin there is being offered to the trade a substitute for menthol made by a firm in Prague which proved to be 80 per cent. acetanilid and oily menthol.

This report consists of 151 pages of interesting matter, the greater part of which is devoted to commercial notes and scientific information pertaining to essential oils; practically every oil used in pharmacy and in the manufacture of perfumery is touched upon as to source of production, supply, and conditions, favorable and otherwise, which may have had some influence on quality or lack of quality.

Considerable attention is given to recent scientific research in

the field of essential oils. Abstracts of reports on experimental cultivation of medicinal plants are given, a field of endeavor which must be nurtured if the supply of drugs is to keep pace with the demand.

Among the pages of this report are several excellent pictures illustrative of the essential oil industry. One is a particularly striking view, in color, of the Miltitz rose-fields at harvest time.

After reading over this report and digesting the information given, one cannot help but feel that in the examination of an oil (say oil of rose) and in which the other constants are normal—a remarkably high ester value should be regarded with suspicion!

BRITISH PHARMACEUTICAL CONFERENCE. A PRESIDENTIAL SURVEY 1863 TO 1913. Being a sketch of the origin and progress of the conference prepared on the occasion of the celebration of its jubilee in London, July 21 to 25, 1913. The Chemist and Druggist, 42 Cannon Street, London.

This handy little volume of 96 pages contains concise but interesting biographies of the various men who have been honored by the presidency of the British Pharmaceutical Conference.

In the fifty years of its existence the Conference has been guided by thirty-three presidents, all men of ability and some of rare scientific attainments. Among the list of names two stand out in bold relief—Hanbury and Attfield. These two names are probably more familiar to workers in pharmacy in this country than any other two from other lands. Hanbury won an enviable position in the world of science by his work as a pharmacognocist. He will also be remembered as the donor of the Hanbury Medal. This is only given to men who have *done* something and our own Professor Maisch was the first American to receive this signal honor. And Attfield, we think few American students are unfamiliar with the book on chemistry bearing that name, with its many chemical experiments which the student is advised to perform. He impressed on the student the fact that the way to study chemistry was to work at it.

JOHN K. THUM.

PAYNE'S DICTIONARY OF PHARMACY. By George F. Payne, Ph.G., M.D., F.C.S. Published by G. F. Payne, Atlanta, Ga.

Lack of space forbids us to give the full title given by the author to this little handbook of pharmaceutical facts. For the same

reason we are compelled to omit mention of the numerous offices and honors the distinguished writer has been honored with and which he mentions on page one. It suffices to say that he is "an active pharmacist for 51 years"; that the little volume is copyrighted, and all rights are reserved, whatever that may mean.

We have been rather hopeful that the day of cramming books was over, but this short-cut to the study of pharmacy and allied branches seems like evidence to the contrary.

The study of a science and art like pharmacy by the "absorption" of isolated facts is a survival of the day when the unschooled errand boy of the retail drug store developed into a clerk and squeezed through a board of pharmacy examination by heroically attempting to memorize the dispensatory. In the past, board of pharmacy examinations consisted very much of "catch" questions and a student expected them and prepared for them; if he answered them correctly the board assumed that he was fit to practise pharmacy; all of which was not conducive to the best interests of the public and certainly lowered the level of the profession. Indeed, the inefficiency of many pharmacists, who must, because of such inefficiency, depend upon manufacturing houses for many pharmaceuticals that they should make themselves, can be traced to this method of education or lack of education in their chosen profession.

Happily, in the larger centres of our country there is beginning to manifest itself by the public a demand for a higher type of man for the professions, ours included. And this demand is being met and complied with by the better class of schools with more stringent requirements as to preliminary education and a broadening of the curriculum. This is as it should be, and in the evolution of things schools of other centres must do likewise or cease to exist.

John K. Thum.

Materia Medica, Pharmacology, Therapeutics, Prescription Writing, for Students and Practitioners. By Walter A. Bastedo, Associate in Pharmacology and Therapeutics at Columbia University, etc.

This book, which is from the press of the W. B. Saunders Co., is a medium 8vo. in size, of 602 pages, price $3.50 net. It is an excellent specimen of the book-making art, the binding and paper being excellent, the type clear and distinct.

The work is original in many respects, not following the beaten path, and has in it much to commend.

It is divided into three parts, Part I being largely by way of introduction. Among some of the subjects considered in this division are: Pharmaceutical preparations; Weights and measures; Active principles; The Pharmacopœia; Dosage, Administration of medicines, etc.

Part II treats of materia medica proper. Many of the classifications are different from other books on this subject, one of them being Sweetening Agents, which includes saccharin, which he states "has been much employed in canning foods, as it is slightly antiseptic and obviates the use of the highly fermentable sugar." This seems to be flying directly in the face of Dr. Wiley. The Anti-Bitters are claimed to abolish the appreciation of bitter tastes; these include yerba santa and gymnemic acid. The list of cathartics include those which act by "selective affinity," as physostigmine, which stimulates the ends of the vagus nerves of the intestines. A new classification is given to the Antispasmodics, they being called the Antihysterics.

The classification of the Antipyretics is somewhat original. We have the analgesic antipyretics, such as antipyrin, the antimalarial antipyretics, such as cinchona; and the antirheumatic antipyretics, such as salicylic acid.

The article on the thyroid gland is interesting and of value, a new classification being called the Antithyroid preparations, designed to overcome undue activity of the thyroid gland, the remedies included under this head being Beebe's serum; Antithyroidin (Moebius), and Thyroidectin. Antithyroidin is the blood serum obtained from sheep whose thyroid glands have been removed, at least six weeks before.

The therapeutic classification of the Disinfectants is also original and valuable. It includes I, The general disinfectants and deodorizers; II, The preservatives; III, Disinfectants for surgical supplies; IV, Disinfectants for local use about the body; V, Disinfectants to be given by the mouth. The important drugs of the materia medica are treated of at considerable length, digitalis having 42 pages assigned to it, and epinephrine (adrenalin) ten pages. In the article on digitalis, it is stated that "digitalis contains digitonin, a saponin body which foams with water and possesses the peculiar property of holding the otherwise insoluble active principles in solution in water. It is on account of this that infusion of digitalis, an

aqueous preparation, represents the activity of the drug." While this is somewhat different from what we have heretofore believed, it does not justify the making of the infusion from a fluidextract, as digitonin is not soluble in an alcoholic menstruum, and such an infusion would not contain any digitonin, and the glucosides insoluble in water would not therefore be held in solution.

The book is up-to-date in the introduction of new remedies, a few only being cited, such as Hormonal from the spleen of the rabbit, which is stated to be "of value in post-operative tympanites and obstinate chronic constipation." Oxyntin and Acidol are albuminous forms of hydrochloric acid. The chapter on Hypnotics is of interest, especially the contrast between natural sleep and that induced by the aid of drugs.

The article on tobacco will be read with interest, as the author seems to think "that the demand for tobacco is not so much the physiological demand of the body for its dose of nicotine, as it is the psychic demand for the satisfaction of a habit."

He thinks that pepsin "in almost all cases of digestive disturbance is a superfluous remedy," but that pancreatin is of greater value. In fact, he gives some remarkable instances of its effects in the case of arrested development, one of which was a boy who grew five inches in two years and gained twenty-two pounds. He is opposed to the prescribing of mixtures of the digestive ferments together, as frequently they destroy each other. Of aconite which has been the sheet anchor of Homeopathy for so many years, is asserted, "that in the light of recent research has doubtful therapeutic value." Camphor cerate is not "camphor ice" as stated, the latter being the Compound cerate of the N. F. Jalap is said to contain 8 per cent. of resin, the amount should be given as 7 per cent. The doses as given in the work vary considerably from those of the pharmacopœia. Under the head of reflex emetics, the dose of copper sulphate is stated as thirty grains, the pharmacopœia gives it as four grains, that of tartar emetic as two grains, the official dose is ½ g.; we have same unpleasant remembrances of the effects of a one-grain dose of tartar emetic. The dose of sparteine sulphate is given as one grain, which is probably nearer correct than the dose given in the Pharmacopœia. The dose of all the mydriatic alkaloids (as atropine) and their salts is stated as the 1/150 grain, no variation between them being given.

Apomorphine hydrochloride is cited as being the only central

(systemic) emetic, other authorities include tartar emetic, senega and squill.

Part III is devoted to Prescription Writing, which the author states "is the dread of the young medical practitioner." This part, while brief, is quite practical, and may be of considerable value in starting the young practitioner aright, but what he should have to make him an expert in the art of prescription writing is a more extensive practice while in college. Much of the fourth year in college could be devoted, directly or indirectly, to this work, and then the young physician would be able to use his knowledge of materia medica intelligently and practically. In conclusion, we would state that we have examined the book with much interest, and shall have pleasure and profit in consulting its pages in the future; it is well worthy of being added to every physician's library.

C. B. Lowe, M.D.

PHILADELPHIA COLLEGE OF PHARMACY.

Minutes of the Quarterly Meeting.

The quarterly meeting of the Philadelphia College of Pharmacy was held December 29th, 1913, at 4 P.M., in the Library. The President, Howard B. French, in the Chair. Sixteen members present. The minutes of the semi-annual meeting held September 29th were read and approved. The minutes of the Board of Trustees, for the meetings held September 2–16, October 7, and November 5, were read by the Registrar, J. S. Beetem, and approved.

Acknowledgments of having received notice of their election to Honorary Membership were received from Doctors Carl L. Alsberg and A. L. Winton.

The President reappointed the following as the Committee on Legislation: Warren H. Poley, Joseph P. Remington, Theodore Campbell, William E. Lee, William L. Cliffe, Richard H. Lackey.

C. A. Weidemann, M.D.,
Recording Secretary.

Abstracts from the Minutes of the Board of Trustees.

September 16th: Thirteen members present. The Committee on Property reported that the Library ceiling had been repaired, woodwork cleaned and varnished, new carpet (cork) put down,

and new chairs purchased. Also that the woodwork of the lower front of the College had been painted, that changes had been made in the lower Microscopical Laboratory, and that the Gymnasium had been put in first class condition.

The Finance Committee approved the recommendation that Prof. Moerk engage the services of two student assistants and Prof. Kraemer one student assistant for the College term.

The Committee on Appropriations approved the estimated amounts that would be required by the several committees and departments authorized to make expenditures.

The Committee on Scholarships.—The Chair reported that owing to the absence of the Dean in Europe, it was necessary to act on the applications presented at the October meeting of the Board and suggested that the Assistant Dean be placed on the Scholarship Committee in the interim. It was so ordered.

The Joint Committee on Instruction and Examination made a report relative to students taking the course in Bacteriology, which was adopted.

The Committee on Examinations reported that John L. Bush, Harry C. Cowles, and Paul A. Kind, having complied with all the requirements, were recommended to receive the Certificate of Proficiency in Chemistry; and that Roy L. Clark having complied with all the requirements was recommended to receive the Certificate of Proficiency in Food and Drug Analysis. These recommendations were approved.

The Committee on Announcement reported the regular issuance of the Bulletin.

A letter was read from the Secretary of the State Pharmaceutical Board relative to the fact that the highest ratings of those who had taken the June examinations had been bestowed upon two graduates of the Philadelphia College of Pharmacy.

Mr. French referred to the honor conferred upon Dr. F. B. Power, a graduate of the College, who had been awarded the Hanbury Gold Medal, and he suggested that a letter of congratulation be sent Dr. Power. This met with hearty approval and the suggestion was adopted.

An application for active membership was received and referred to the Committee on Membership.

The Treasurer's Annual Report was received, and referred to the Committee on Accounts and Audit.

October 7th: Thirteen members present. A communication was received from the Recording Secretary of the College reporting the election of E. M. Boring, Charles Leedom, and Theodore Campbell to membership in the Board of Trustees for the ensuing three years.

The Committee on Property reported that the back hall and stairway had been painted and put in good condition.

The Committee on Library reported that up to this time 5246 books had been classified, accessioned and shelf-listed.

Donations of books had been received from H. G. Kalmbach, Mrs. Wm. McIntyre, Professor C. B. Lowe, Professor Henry Kraemer and the Surgeon's General Office. A number of books had been purchased. Fifty-two persons had used the Library.

The Committee on Instruction reported that several students had removed conditions, and that several others still had conditions to be removed, and suggested rules to govern such cases in the future; also that Prof. Kraemer had selected Anton Hogstad, a third year student, as an assistant.

The Chairman stated that Professor Roddy had requested Messrs. Mulford & Company and Parke, Davis & Company to present samples of Bacteriological products to his laboratory, with which request they had complied and new products would accordingly be added. The thanks of the Board was conveyed to the donors.

The Committee on Scholarships reported the names of twelve persons to whom scholarships had been awarded.

Mr. Shoemaker read a communication from Prof. Kraemer to the Registrar relative to the fund started by the classes ending in 4 and 9, to the effect that the fund be placed in the hands of the Treasurer. The Treasurer suggested that the fund be one representing all graduates. Prof. Kraemer was requested to outline the plan undertaken by the classes and to submit such outlined plan at the next meeting of the Board.

An application for Associate Membership was received and referred to the Committee on Membership.

The Committee on Membership reported favorably on the application of George L. Sontag, of Neillsville, Wisconsin, Class of 1890. A ballot was taken and he was unanimously elected.

November 5th: Thirteen members present. Committee on Library reported an additional number of books accessioned, classified and shelf-listed and that a gift had been received from G. Mason Thompson. A number of books had been purchased. One hundred and forty-six persons had used the Library.

Committee on Instruction reported that the Sub-Committee on Special Lectures had secured outside talent to deliver nine special lectures during the College term. A wide range of subjects having been selected. Several joint meetings of the Committees on Instruction and Examinations were held to formulate some system of grading or evaluation to be attached to the results of the examinations in the various branches of the College—such system that differentiates between the Major and Minor branches. After earnest consideration, a plan has been proposed by which each subject of instruction will be given a rating corresponding with its importance. This plan will be put in force for the present year in order that its adaptability to the conditions now existing may be tested.

The Secretary announced that he had received letters from the recipients of scholarships expressing their appreciation.

The Chairman read a letter from Dr. F. B. Power expressing his appreciation of the good wishes and congratulations extended him by the College. The correspondence was directed to be published in the AMERICAN JOURNAL OF PHARMACY.

PHILADELPHIA COLLEGE OF PHARMACY.
September Twenty-third, 1913.

DR. FREDERICK B. POWER,
Snow Hill, London, E. C., England.

Dear Doctor:

The news that the Committee on Hanbury Medal of the Pharmaceutical Society of Great Britain had awarded you this year this coveted medal, has been received by the members of the Philadelphia College of Pharmacy with mingled feelings of pleasure and pride. It is now nearly forty years since your first scientific papers were published in our JOURNAL and we appreciate that with the harvest of material that is yours, you still remember us. It is but natural on an occasion of this kind, being probably the proudest in your life, that we in offering you our felicitations and congratulations should remind you that the successive steps in your career since graduating from our College and working in its faculty, have been followed by us with increasing interest as year by year has passed. Rarely does it fall to the lot of any one man to accomplish so much, and it is even more unusual for him to receive while yet in his prime, the recognition he deserves for the days and nights of unremitting

toil with which he has applied himself to his chosen task. We trust that you may be spared many years to continue your studies, and it is our earnest desire that the harvest may satisfy your proudest hopes and highest expectations. We wish you health that you may work easily as well as effectively and enjoy the fruits of your labors.

Very truly,

HOWARD B. FRENCH,

President.

THE WELLCOME CHEMICAL RESEARCH LABORATORIES,
FREDERICK B. POWER, PH.D., LL.D., DIRECTOR.

6, King Street, Snow Hill, London, E. C.
13 October, 1913.

HOWARD B. FRENCH, ESQ.,
President, Philadelphia College of Pharmacy,
Philadelphia, Pa.

Dear Mr. French:

It has given me exceptional pleasure to receive your very kind letter of the 24th ultimo, and I desire to assure you of my deep appreciation of the cordial sentiments and good wishes therein expressed.

The significance of the honor attending the award of the Hanbury Gold Medal has been greatly enhanced to me by the feeling that its bestowal has also afforded gratification and pleasure to so many of my esteemed friends across the sea. The occasion of its presentation on October 1st was a memorable one, and it was a great delight to me, as indeed to the entire assembly, that Professor Remington could be present and participate in the proceedings. His remarks in seconding a vote of thanks, proposed by Sir William Tilden, F.R.S., for my address, were most felicitous, and it was altogether a grand and happy day.

I have been deeply touched by the expressions of interest manifested in my career by the Philadelphia College, which has indeed been to me a "kindly mother." I am grateful for the stimulus to scientific study which was first received as a student within its walls, and appreciate very highly the honors it has in later years conferred upon me.

In heartily reciprocating your good wishes for health and happiness, believe me to be,

Sincerely yours,

FREDERICK B. POWER.

The Committee on Membership reported favorably on the application of Otto Raubenheimer, of Brooklyn, N. Y., as an Associate Member. A ballot was taken and he was unanimously elected.

PHARMACEUTICAL MEETINGS.

The second Pharmaceutical meeting was held on Friday afternoon, November 14, Mr. Edward M. Boring presiding.

Prof. Charles H. LaWall presented a paper on "Detection of Chicory in Decoctions of Chicory and Coffee" prepared in conjunction with Mr. Leroy Forman.

Mr. Boring then exhibited two specimens of Elixir of Iron, Quinine and Strychnine, made six months apart, their fine appearance being due to neutralization after the addition of the iron phosphate.

Prof. Remington gave a delightful talk on "Some Pharmaceutical Celebrities I Have Met," in connection with which he showed a large number of slides including portraits and views in laboratories abroad and in manufacturing houses.

OBITUARY.

EVAN TYSON ELLIS was born in Philadelphia on August 10, 1826 and died in the same city on October 11, 1913. He was the oldest alumnus and member of the Philadelphia College of Pharmacy, the last surviving charter member of the Philadelphia Photographic Society, and for many years a prominent figure in the wholesale drug circles of Philadelphia.

Mr. Ellis came of sturdy Quaker stock, his father, Charles Ellis, being a well known Orthodox Quaker, a leading wholesale druggist and an official, in various capacities, of the Philadelphia College of Pharmacy for more than forty years. He received his education at Haverford College from which he was graduated with the class of 1844 and was one of the oldest members of the Haverford College Alumni Association. He then studied pharmacy, attended the courses of instruction at the Philadelphia College of Pharmacy, graduating with the class of 1847. The subject of his thesis was "Extract of Valerian."

After he was graduated, Mr. Ellis went into partnership with his father, Charles Ellis, in Philadelphia, and together they built up a large wholesale drug business, under the name of Charles Ellis, Son and Co. During the Civil War he served in the Hospital Department of the U. S. Army.

J. W. ENGLAND.